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**Figure 1**

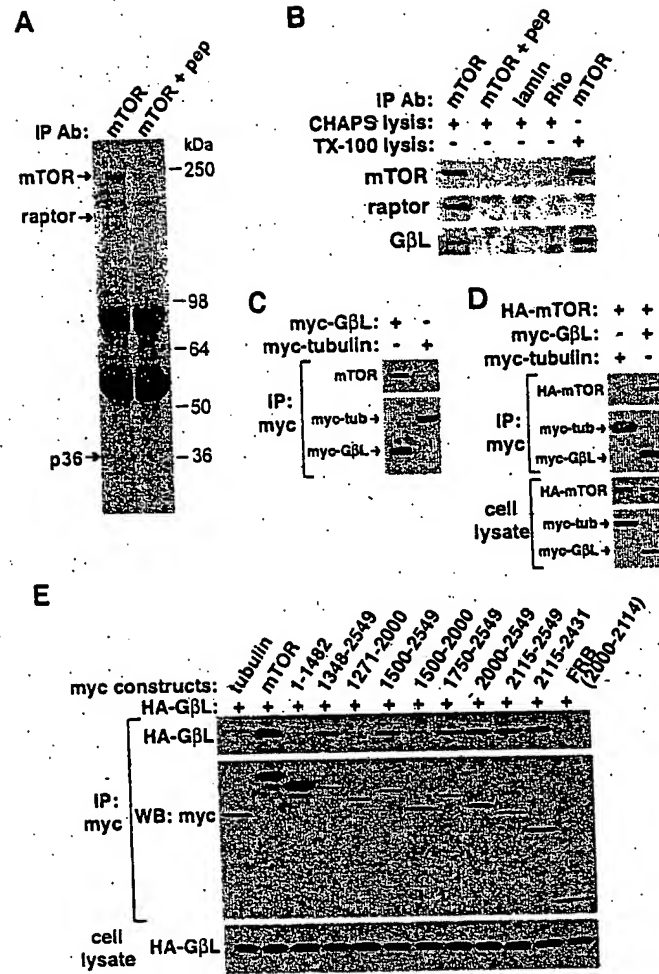


Figure 2

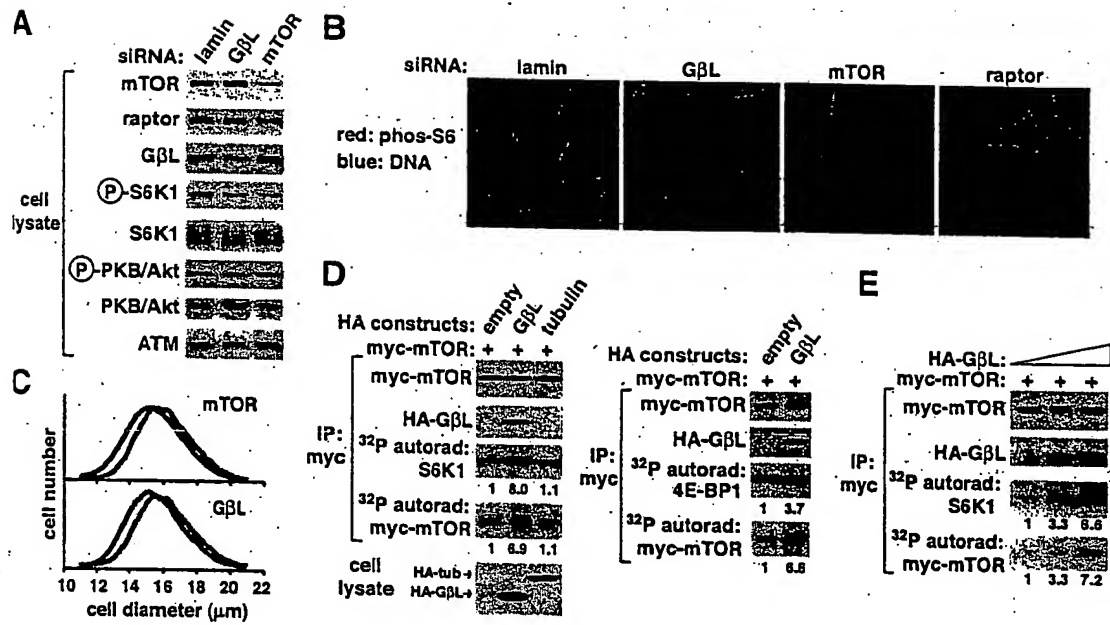


Figure 3

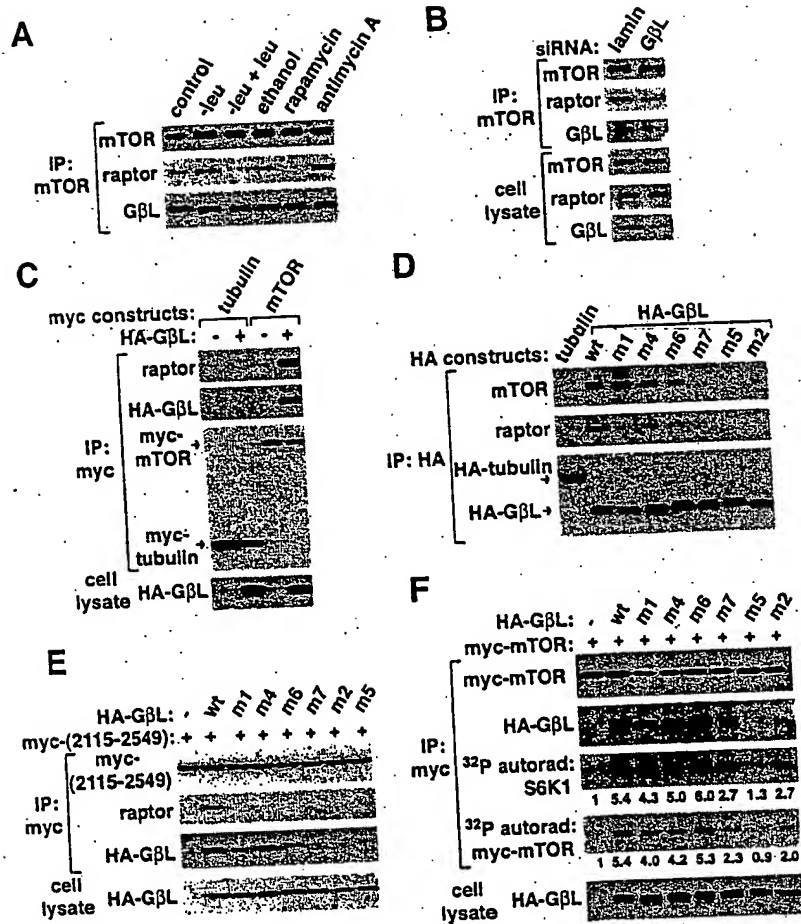


Figure 4

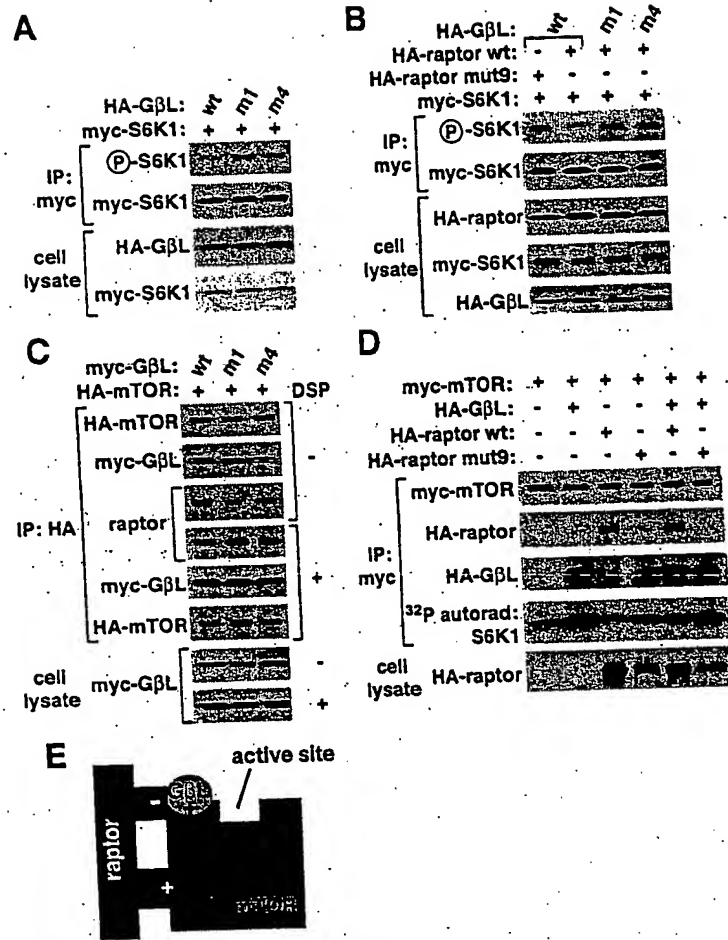


Figure 5a

p200 mRNA sequence (i.e. includes UTRs and ORF)  
AGCGGGTTGTGACTGAACCCCGTCAATATGGCGGGGATCGCGCGCGCGCTCTCTGAAGAACCTCCGAGTACGAGGGCG  
GAATGACAGCGCGGAGAGAACGTCCCGTGGATCTGACCCGAGAACCTTCTGATAAATTAAGAGAGATTCCTCCAAAATG  
TGGCCAGATTGCAGGGAGTATCAAAATAGAGAAAGCTAGGCCATCTGAATAACTTTTACTAAGCTTCTTTGTGATATTGGC  
CACAGTGAAGAAAACCTGGGCTTTTCACTATGAGGATATCATAAATTTGTGCGGTAGCTTTATTAATAAGAAAGCAAAAGA  
AGTGGGAGCAGCAGGGCTACGAGGCTTCGATATCTCATCCAAAGACTCCAGTATTTCTCCAGAAAGGTGCTAAAATTTGAAAAG  
TGGACTATTTAAATAGCTAGGTGCATTCGATATGACATACAAACAGAGCAACGAGGTAGAGAGGACACAAAGCACTTCGATTAGTCAGA  
AAGATGATTACTGTGAATGCTTCCCTTGTTCCTAGTTCCTGTGACCAACTCATTAATTGCAGTTGGAAATGATGGACTTTCA  
AGAAAGAGACAGAATGGTCCGAGCATGCAATGCCATTTATCTGTGAACCTAGCACTTCAGAAATCCAGAGGTGGTGGCCCTTC  
GAGGAGGACTAAACACCATATTTGAAAATATGTGATTTGATTTGCCAATTAAGTCCGAATAAATGAGGCCCTTAATTACTACAAAT  
TTGCACCTTCTTAATCATCCAAAGACTCGGCAGTATGTGCGAGCTGATGTAGAAATTAGAGSAAATTTTAGCACCCCTATAC  
TGATTTTCACTACAGACATAGTCCAGATACAGCTGAAGGACAGCTCAAAAGAACAGAGAACAGCAAGCAAGATTTCTAGCCAGTA  
AAATGGGAATCATAGCAACATTCGGATCATGGGCAAGTATTAATTAATTTATGTAAACCTGGAAATTTATGATATAATTTCTGCTCTTC  
CTAATAGGAGTACTTTGCATACCAAAATATGAAATAGGCGAGGTCTACTAGTGTAGATCCAGGGAGGTTCCTAAGACAGTTGGAGGCTTT  
TCTACCTGTGTGACTGAGGAGTTCTATAGAACACACTACTCAGTGTAGATCCAGGCCAGACCTCATGGATAAATTAAT  
CAGATGGCTTTGTGGCAGCTGAGGCAAAAATATTTCTTCTCATCGTGCAGATCCAGGCCAGACCTCATGGATGATGATCA  
TTGGCACITGATCTCTGCAATTTATTCGTAATGGACTTTTAGAGGGTCTAGTCCGAAGTGAATAACAAACAGTGTGATGATCA  
TATCTCAGTTAGAGCTACCATCTTTTAGGAGAGCTTTTACATATGGCAAAACACAATTTCTTCTCATTCACATAGCCATC  
ATTTACACITGCTTGCCAAACCCTAATGAATATGGCTGCATCTTTTGATATCCCCAAGGAAAAGAGACTGCCAGCCAGTGCA  
GCCTTGAACCTGTTTAAACGCTTCCATGAAATGAAGAACGAGGACCTAAGCTTTATAGTCTTTCATTTAGACCACATTAAT  
TCAGAAAGCAATTGCAACACACACAGAAACGGGATCAGTATCTCCGAGTTTCAGAAAGATATAATTTATCTTAAGGATACAG  
AGGAAGCTCTTTTAAATTAACCTTAGAGATAGCCAAAGTCTTCAACATAAAGAGAAATCTTTGAATGGAAATTTGGAATCTTTATA  
GGGACCATTTTAAAGTGGCCAAATGTAAATCTAAAGAACTATAAGATGAACAGTTACACAGGTTTGTACGAAGACTACT  
TTATTTTACAAAGCCAGCAGTAAATTAATATGCCCACCTGGATCTGGATTTTGCCAAAGGCCAAACAGCTCACGGTTGTAG  
GTTGCCAGTTTACAGAAATTTCTTCTTTGAATCTGAAGAGGATGGCAAGGCTACTTAGAAGATCTAGTAAAGGATATTGT  
CAGTGGCTCAATGCTTCATCTGGAAATGAACCCGAAAGAGTCTTCAAAATATAATGGTTTATTTGACCACCTTTAGTCAACA  
CTACTTTTATTTATTTGGAACACTTTCTTGCCACCTCATGGAGTTAAATATGCTGGAAAAATGCACTGTATTTTCAGTGT  
TCCTTAATCTTTTGTCTCTTGAAAAAACCAAGATCACTTGCTTAAACTTACTGTCTTAGCTTGGACTATAGCAGAGATGGA  
TTGGCTAGAGTATCTTTTCCAAAATTTTAACTGCAGCTACTGATGCCCTGCAGACTCTATGCAACAAAAACATTTTAAAGGT

Figure 5b

ATTATTGAGAGCTAATGTTGAATTCCTTTAAATAATTGGGGAATTGAGTTGTTAGTGACCCAGCTACATGATAAAAAACAAA  
CGATTTCCCTGAAGCTCTTGATATCCCTCGATGAAGCATGTGAAGACAAGGCCAATCTTCATGCTCTCATTCAGATGAAA  
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GAATGAAAGAGGTTATGTAGCAAAAACAATTGGAAAAGTGGCACAGGGAATACAACTCCAAAATATGTTGACTTGATTGAGG  
AACAACTCAATGAAGCACTTACTACTTACCGGAAGCCTGTTGATGGTGATAACTATGTTCTGTCGGAGTAACCAAAAGATT  
CAGCGTCTCACGTCFACCTGCTTATACACCTTTATGGACAACTAGTACACCAATTTGGATAAGTGGGAAGAAATTAATAA  
ACAGAAATATTATACAGAACTCTGTCGTAATGTTCCATCAATGCGGCTCATCAAAATGCGGCTCAAGGAAACGTTGATTC  
CATCTTTTGGGCTTGGGAAATATCGGCTCATCAAAATGCGGCTCATCAAGGAGGACCTGTGTATATGTAATGTAATGTA  
ATACTAAAACCTTGCAAAACAGTGTGAAGTTCTTTCCATCAGAGGGACCTGTGTATATGTAATGTAATGTAATGTAATG  
CAACAAGGCTGTGATATTCTTAAATGTCAAACTGGGATGCTGTGAGGCATAGTCGCAAAACATCTGTGGCCAGTGGTTC  
CAGATGATGTGGAACAACCTCTGTAAATGAACCTTTCACTATCCCAAGCACTTAAGTTTGAACCTCGGAGTCAACCACT  
AGACATAATAGTGAAGTGAATCTGTGCCATCGAGTATGTTCAATTTGGAGGATGACCGGTTTGGCAGCAGCTCTACTAG  
TACATTTTCTTGTGATATCAATGAAGATACAGAGCCAAACATTTATGACCGATCTGGACCCATAAAGGATAAAAAATTCAT  
TCCCCTTCTTGTCTTCTAGTAAACTTTGTGAAGAACTCGTATCTTTAAATTCGCTTACTTTGCTTAAACAAAAACATCTG  
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TGTTGATTTTAAATCATAGTGAATTTTACACCCATATCCACTGTACAGAAAACATGACTTAAATTCACCAAGAAATTTT  
GGAATAAGCACATTGAAGACACTGGTAGTACACCAAGCATTTGGAGAAATGACTTAAATTCACCAAGAAATTTTGGTACA  
GAGAAATCAGAGAAATATACAAGCCGAGAGAGGTTAGTAGAAGAAAGTTCAAGCTCCTTACGAGAGACAGTAGGTGTAGATG  
AAGTTTCAATACAGACACTACAACAAGTGGCATAAAGTTCAATGAGCTCAAGTCTTACGAGAGACAGTAGGTGTAGATG  
CTACAACATATGGACACAGACTGTGGAGCATGAGTACTGTGGTAAGTACTAAAACATATTAAGACAAAGCCACTATTGACG  
CCACAGTCTAACCATCTGTCTCTCTCCAAATCAAAATTCGGTGTCCCTGGTGCTCCAGGTTCTTCTCATACGCTTCTCTAG  
AAGAGCACAGTCCCCTTAAAGCACCCCTCTATTGCTACAAATTAAGTCTAGCAGATGTAACTTTAGTTACACAAGTTCTTA  
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GCATCTCCAGCAAAAGATGTGCTATTACTGATACCATCAATGAAGGCCAACAGTTTGTAGTCCAGATTAACACCAAG  
CAGGTTCAAGAACCTTAAGTTATGCTATAGATTAAGAAAGATTTATTTAGTCTTATTTAGTCTTCTCTCCCGGTG  
GATCTTCTCAGTCCGCTCCATGGTGTCCAGTGCCACATATGGGGTTTCAGATGATTAACATACCACCATGATCGAGGTGC  
GATATAAATGATATATTCCAGGTAAAGGATATTCCCTATTTCAGACAAAAAATTTCTTTTCACTTGTCTACGAC  
AAGAGCATTTTGCCCATGATGCAGGAGGCTTTCCATCTGGAACCTGGAGGCTTTGTAAAAAATTTCTTTTCACTTGTCTACGAC  
AGCAGATGAGTCTTACGGAAATAAATGAATTCATCCATTCAGATGCCCTCTCTGTTTGTAGAAAAGTACAGAAAGACACTGGA  
CTACAGGAACATACAGATGATAACCTGCTTTTATTTGTGCTGTATTTGAATTTCTGGGTTTTCAGCCCAAGCAACCACTGAG  
TGCAATATGTAGTCAATTCAGACTTTTCAAGATATTTCCATATTTCTGATTTGGTGTGAGCAGACTATCCATAATCTTTAGAA  
TGGTTCCCCTCTAAAGTTTTCGGGGAATTTCTGGATGCGAGTGTGGGTGTCTCAAGAAAGGCTCAGCTAGCAGCACCAAAAGC

Figure 5c

ACAGAAATTGTTACTAGGTGTTAAACAATTCCAGATGATACACCAATGTGCCGTATACTCCTTCGCAAGAAGTTCTTAAG  
ATTAGTCATTAAATTGAGTAGTTTCAGTTTCAACTAAATGTCA TGAGACTGGGCTTTTAACAAATTAAAGGAGAAAGTATCCTC  
AAACATTTGATGACATATGCCCTTTACTCTGAGGTTTCCCATTTGCTGTCACTGCACATTCAGACTTCCCGTGTGCGAGG  
TTCATACAAAGAATTATTTCAAGATGTACAGTTTCTACAAATGCATGAAGAAGCAGAGGCTGTGTGGCAACACCCACCAAA  
GCAACCTATAGTTGATACATCTGCTGAATCCTGACCTCATATTTATGATGGATATAGATACATATATATATATATTCATAT  
TTGTGGATTTCCTAAAGCCTCAGAAAAATACGACTGACTAGGCAGCAAGACAGGATATCTTCTGTACACTGTGTCCGCA  
GTTACTGGTACATGAACAGTTGGAACTGCTGACTTTCCTAACCAAAACAACCTTCTCTCCTTTGTGTGAGCCCTTTTGA  
GGGTTTCATGATTCATTACCACAGTTTAAAGAGTTTTCAGTTTACCATTGTATGCAAGAGCCCAAGCACTGAATACCTACATA  
GGTTTTCATATTTTCTTTTCAATTTTAAAGCGTAATGACAGTGGAAACAATAATGGGATATGCAGAAAGCACCCCTTCACAAGTT  
ATTCTGAATGATTTTAGGGTAAATAATACAGATGCCCTTGTATGTTAACTAACTTGTGGAAGCAGGAATCAGTGTCTCT  
AAGGCTGCATCCTATTACCACAAATGGGGTTGTGCTATACTGGCTGGTATTAGAGAGGGAAC



Figure 6a

p200 ORF sequence (i.e., no UTRs)  
ATGGCGCGATCGCGCGCGCGCTCTCTGAAGAACCCTCCGAGTACGAGGCGGGAATGACAGCGCGGAGGAGAACGTCCC  
GCTGGATCTGACCCGAGAACCTTCTGATAACTTAAGAGAGATCTCCAAAATGTGCCAGATTGACGGGAGTATCAATA  
TGAGAAAGCTAGGCCATCTGAATAACTTTACTAAGCTTCTTTGTGATATGGCCACAGTGAAGAAAAAATGCGCTTTTCAC  
TATGAGGATATCATAAATTTGTTTGGGGTTAGCTTTTAAATGAAGCAAAAAGAGTCCGAGCAGCAGGGCTACGAGCGCT  
TCGATATCTCATCCAGACTCCAGTATTTCTCCAGAGGTGCTAAAATTGAAAGTGGACTATTTAATAGCTAGGTGCAATTG  
ACATACAACAGAGCAACGAGGTAGAGAGGACACAGCACTTCGATTAGTCAGAAAAGATGATTTACTGTGAATGCTTCCCTTG  
TTTCCCTAGTTCTGTGACCAACTCATTAATTCAGATTGCAAGTTGGAATGATGGACTTCAAGAAAGAGACAGAAATGGTCCGAGCATG  
CATTGCCATTATCTGTGAACCTAGCACCTTCAGAACTCAGAGGTGGTGGCCCTTCGAGGAGGACTAAACACCATATTGAAAA  
ATGTGATTGATTGCCAATTAAAGTCGAAATAAATGAGGCCCTAAATTACTACAAATTTGCACCTTCTTTAATCATCCAAAGACT  
CGGCAGTATGTGCGAGCTGATGTAGAAATTAGAGSGAAATTTAGCACCTTATCTAGTATTTTCACATACAGACATAGTCCGAT  
TACAGCTGAAGGACAGCTCAAAGAAGACAGAGAACGACGATTTCTAGCCAGTAAATGGGAATCATAGCAACATTCGGAT  
CATGGGCAGGTATTATTAAATTTATGTAAACCTGGAAATTTCTGGGATCCAGTCTCTAATAGGAGTACTTTGCAATACCAAT  
ATGGAAAATAAGGCGAGGTCTACTTTGAAGTGTCTTTATGATATATTTCTGCTTCCCTCTACCTGTGTGACTGAGGAGTTTCAT  
AGAAGCACTACTCAGTGTAGATCCAGGAGGTTCGAAGACAGTTGGAGGCTTTTCAGATGGCTTTGTGGCAGCTGAGGCAA  
AAACTATTCTCTCTCATCGTGCAGATCCAGGCCAGACCTCATGGATAATTATTGGCACTGATCTCTCTGCAATTATTT  
CGTAATGGACTTTTAGAGGGTCTAGTCGAAGTGATAACAAACAGTGTGATCATATCTCAGTTAGAGCTACCATCTTTT  
AGGAGAGCTTTTACATATGGCAAAACAAATTTCTCTCATTTACATAGCCATCATTTACACTGCTTGCCAAACCTTAATGA  
ATAATGGCTGCATCCCTTTGATATCCCCCAAGGAAAGAGACTGCGAGCCAGTGCAGCTTGAACCTGTTTAAAAACGCTTCCAT  
GAAATGAAGAAACGAGGACCTTAAGCCTTATAGTCTTTCATTTAGACCACATTTATTCAGAAAGCAATTGCAACACACCCAGAA

Figure 6b

ACGGGATCAGTATCTCCGAGTTCAGAAAAGATATATTTATCCTTAAGGATACAGAGGAAGCTCTTTTAAATTAACCTTAGAG  
ATAGCCAAGTCTTCAACATAAAGAGAAATCTTGAATGGAATGGAATCTTTATAGGGACCAATCTTAAGTGCCCAAATGTA  
AATCTAAGAAAACCTATAAAGATGAACAGTTACACAGGTTTGTAACGAAAGACTACTTTATTTTACAAAGCCAGCAGTAAAT  
ATATGCCAACCTTGGATCTGGATTTTGGCAAGGCCAAACAGCTCACGGTTGTAGGTTGCCAGTTTACAGAAATTTCTTCTT  
AATCTGAAGAGGATGGCAAGGCTACTTTAGAAAGATCTAGTAAAGGATATTTGTTCAGTGGCTCAATGCTTTCATCTGGAATG  
AAACCCGAAAGAAAGTCTTCAAAAATAATGGTTTATTTGACCCACCTTAGTCAACACACTACTTTTATTTATTTGGAACACTTTC  
TTGCCACCCCTCATGGAGTTAAATGCTGGAAAATAATGCAGTGTATTTTCAGTGTCTCTTAAATCTTTTGTCTCTTGAAAAACC  
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TTAACTGCAGCTACTGATGCCGTCAGACTCTATGCAACAAAACATTTAAAGGTTATTTATTTGAGAGCTAAATGTTGAATTTCTT  
TAATAATTGGGGAATTTGAGTTGTAGTGACCCAGCTACATGATAAAACAAACAGATTTCTCTGAAAGCTCTTGAGATATCC  
TCGATGAAGCATGTGAAGACAAGGCCAATCTTTCATGCTCTCATTTAGATGAAACACAGCGTTATCCCACTTGGAGACAAG  
GGTTTGTCTTCTCCTGCTGAGATTTCTCTCCATTTCCAAAAGGATTTTCTCTATCTGAATGAAGAGGTTATGTAGCAAAACA  
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ACCGGAAGCTTGTGATGGTGATAAATGTTGTTGCTGGAGTAACCAAGATACAGCGTCTCACGTTACCTGCTCTATA  
CACCTTTATGGACAACACTAGTACACCAATAAAGAGGCTGCCATTTGTTGGAAGTACAGAAATATTTATACAGAACTCTGTGCG  
TAATGTTCTGTACACCAAGATTTGGATAAGTGGGAAGAAATTAATAAATCTGAAAAGCATCTCTTTGGGCCCTTGGGAAAATATCG  
GCTCATCAAAATTTGGGCTCTCAATTTGCTACAGGAAGAAAACGTTGATTTCCAGATATCTAAACCTTGCAAAACAGTGTGAA  
GTTCTTTCCATCAGAGGGACCTGTGTATATGTTACTTTGGCTCATAGCTAAAACCAACAAAGGCTGTGATATTTCTAAATG  
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AACTTTTCATCTATCCCAGCATCTFAAGTTTGAACCTCGGAGTCAACCAAGCTCTAGACATAATAGTGAAGTGAATCTGTG  
CCATCGAGTATGTTTCATATTGGAGGATGACCGGTTTGGCAGCAGCTCTACTAGTACATTTTCTTCTTAGTAAACITG  
TACAGAGCCCAACATTTTATGACCGATCTGGACCCCATAAAGGATAAAAAATTCATTTCCCTTTCTTTGCTTAGTAAACITG  
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TCATCTGAAAGTAAGACAAGCAACAGCGGAATCAGAACACTTACGGAGCCAGTGTGATTTTAAATCATAGTGTGATTT  
TACACCCATATCCACTGTACAGAAAACATTAACAATTAGAGACTTCTATTTATGGGAATAAGCAGACTTGAAGACACTGGTA  
GTACACCAAGCATTTGGAGAAAATGACTTAATAATTCACCAAGAAATTTTGGTACAGAGAAATCACAGAGAAAATACAAAGCCGA  
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GCATGAGTACTGTGTAAGTACTAAACTATTAAAGACAAGCCACTATTTGACGCCACAGTCTAACCATCTGTCTCTCTCC  
AAATCAAAATTCGGTGTCCCTGCTCCAGGTTCTTCTCATACGCTTCTTAGAAGAGCAGTCCCTTAAAGCACCCTC  
TATTGCTACAAATTAAGTCTAGCAGATTTGTAACCTTAGTTTACAAAGTTCTAGAGATGCTTTTGGCTATGCTACACTGA  
AAAGACTACAGCAACAAAGAATGCATCCATCTTATCTCACTCTGAAGCTTTTGGCATCTCCAGCAAAAGATGTGCTATTT

Figure 6c

ACTGATACCATCACCATGAAGGCCAACAGTTTGTGAGTCCAGATTAAACACCAAGCAGGTTTCATGAAAAGCCTTAAGTTATGCA  
ATCATTAGATAAAGAAAGATTATTTGAGTCCCTATTAATCAAAATACCCCTGCAACGATCTTCCCTCAGTGCAGTCCCATGGTGT  
CCAGTGCCACATATGGGGTTCAGATGATACATTTGGTCTTGGCTCTCCCGGTGGATATAAATGATATATCCAGGTAAAG  
GATAATCCCTATTTTCAGACAAAACATACACCAACATGATGATCGAGGTGCAAGAGCATTTGCCCATGATGCAGGAGG  
TCTTCCATCTGGAACTGGAGGTCITGTAAAATTCITTTTCACTTGTCTACGACAGCAGATGAGTCTTACGGGAAATATATGA  
ATTCAATCCATTAGATGCCCTCTCTGTTTTGTAGAAAGTACAGAAAGACACTGGACTACAGGAACATACAGATGATAACTGC  
CTTTATTTGTGTCTGTATTGAAATTTCTGGGTTTCCAGCCCAACCACTGAGTGCATATGTAGTCAATTCAGACTTTTCA  
AGATATTCCATATTCTGATTTGGTGTGAGCAGACTATCCATTAATCTTTAGAAAGTGGTTCCCTCTAAAGTTTTCGGGGATTT  
CTGGATGCAGTGATGGGGTGTCTCAAGAGGTCAAGCTAGCAGCAACCAAGCACAGATTTGTACTAGGTGTTAAACA  
ATTCCAGATGATACACCAATGTGCCGTATACCTCTCGCAAGAAAGTTCTAAGATTAGTCAATTAATTTGAGTAGTTCAGT  
TTCAACTAAATGTCAATGAGACTGGGCTTTTAAACAAATTAAGGAGAAAGTATCCTCAAAACATTTGATGACATATGCCCTTTACT  
CTGAGGTTTCCCATTTGCTGTTCACACTGCACATTCAGACTTCCGTGTCCGAGGTTTCATACAAAGATTTATTTCAAGATGTA  
CAGTTTCTACAAATGCAATGAAGAAGCAGAGGCTGTGTGGCAACACCAACCAAGCAACCTATAGTTGATACATCTGCTGA  
ATCCTGA

Figure 7a

p200 amino acid sequence  
MAAIGRGRSLKNLVRGRNDSGEENVPLDLTREPSDNLREILQNVARLQGVSNMRKLGHLNNFTKLLCDIGHSEKLGPH  
YEDIIICLRALLNEAKEVRAAGLRALRYLLIQDSSILQKVLKVDYLIARCDIQQSNVERTQALRLVRKMITVNASL  
FPSSVTNSLIAVNDGLQERDRMVRACIAIICELALQNPEVVALRGGLNTILKNVIDCQLSRINEALITITILHLNLNHPKT  
RQYVRADVELEXILAPYTDHFYRHSPTAEGQKEDREARFLASKMGIATFRSWAGIINLCKPGNSGIQSLIGVLCIPN  
MEIRRGLEVLVDIFRPLPVVTEEFIEALLSVDPGRFQDSWRLSDFVAEEAKTILPHRARSRPDLMDNYLALILSAFI  
RNGLLEGLVEVITNSDDHISVRATILLGELLHMANTILPHSHSHLHCLPTLMNMAASFDPKEKRLRASAAALNCLKRFH  
EMKKRGPKPYSLHLDHIIQKAIATHQKRDQYLRVQKIDIFILKDTTEALLINLRDSQVLQHKENLEWNWNLIIGTILKWPNV  
NLRNYKDEQLHRFVRRLLYFYKPPSSKLYANLDDLDFAKAKQLTVVGCQFTEFLLSEEDGQGYLEDLVKDIVQWLNASSGM  
KPERSLQNNGLLTTLISQHYFLFIGTLSCHPHGVKMLEKCSVFQCLNLCSLKNQDHLLKLTVSSLDYSRDGLARVILSKI  
LTAATDACRLVATKHLRVLRLANVEFFNNWGIELLVTQLHDKNKTISSSEALDILDEACEDKANLHALIQMKPALSHLGDK  
GLLLLRFLSIPKGFSYLNERGYVAKQLEKWHREYNSKYVDLIEEQNEALTTRYRKPVDGDNVYVRRSNQRLQRPHVYLP  
HLYGQLVHHKTGCHLLEVQNIITELCRNVRTPDLDKWEELKKLKAASLWALGNIGSSNWGLNLLQEEENVIPDILKLAKQCE  
VLSIRGTCVYVVLGLIAKTKQGDILKCHNWDVAVRHSRKHLPWPVPPDDVEQLCNELSSIPSTLSLSESTSSRHNSESESV  
PSSMFIEDDDRFGSSSTSTFFLDINEDTEPTFYDRSGPIKDKNSFFFASSKLVKNRILNSLTLPNKKHRSDDPKGGKL  
SSEKTSNRRIRTLTEPSVDFNHSDDFTPISTVQKTLQLETSMGNKHIEDTGSTPSIGENDLKFTKNFGTENHRENTSR  
ERLVVESSTSSHMKIRSQSFNTDTTTSGISSMSSSPSRETGVGDATMTDTCGSMSTVSTKTIKTSHYLTPQSNHLSLS

Figure 7b

KNSVSLVPPGSSHTLPRAQSLKAPSIATIKSLADCNFSYTSSRDAPGYATLKRLQQQRMHPSLSHSEALASPAKDVLF  
TDTITMKANSFESRLTPSRFMKALSYASLDKEDLLSPINQNTLQRSSVRSMVSSATYGGDDYIGLALPVDINDIFQVK  
DIPYFQTKNIPPHDDRGARAFADAGGLPSGTGGLVKNSFHLRLRQQMSLTEIMNSIHSDASLFLESTEDTGLQEHDDNC  
LYCVCIEILGFQPSNQLSAICSHSDFQDIPYSDWCEQTIHNPLEVVPSEKFSGISGSDGVSEGSASSTKSTELLGVT  
IPDDTPMCRILLRKEVLRLVINLSSSVSTKCHETGLLTIKEYPQTFDDICLYSEVSHLLSHCTFRLPCRRFIQELFQDV  
QFLQMHEEAEAVLATPPKQPIVD TSAES.

## Figure 8

[illegible]

Figure 9a

GβL ORF sequence (i.e., no UTRs) (derived from accession # BC017119)  
ATGAACACCTCCCCAGGCACGGTGGGCAGTGACCCGGTCAATCCTGGCCACTGCAGGCTACGACCACACCCGTGCGCTTCTG  
GCAGGCCACACAGCGGCATCTGCACCCGGACGGTGCAGCACCCAGGACTCCCCAGGTGAATGCCCTTGGAGGTACACCCGGACC  
GCAGCATGATTGCTGCTGCAGGTTACCAGCACATCCCGCATGTATGATCTCAACTCCCAATAAACCCCTAACCCCATCATCAGC

Figure 9b

TACGACGGCGTCAACAAGAACAATCGCGTCTGTGGGCTTCCACGAAGACGGCCGCTGGATGTACACGGGGCGGAGGACTG  
CACAGCCAGGATCTGGGACCTCAGGTCCCGGAACCTGCAGTGCCAGCGGATCTTCCAGGTGAACGCACCCATTAACTGCG  
TGTGCCCTGCACCCGAACCAAGGCAGAGCTCATCGTGGGTGACAGAGCGGGGCTATCCACATCTGGGACTTGAAAAACAGAC  
CACAAACGAGCAGCTGATCCCTGAGCCCGAGGTCTCCATCACGTCCGCCACATCGATCCCGACGCCAGCTACATGGCAGC  
TGTCATAATAGCACCCGAAACTGCTATGTCTGGAACTTGACGGGGGCAATTGGTGACGAGGTGACCCAGCTCATCCCCAAGA  
CTAAGATCCCTGCCACACGCGCTACGCCCTGCAGTGTGCTTCAGCCCGACTCCACGCTCCCTCGCCACCTGCTCGGCT  
GATCAGACGTGCAAGATCTGGAGGACGTCCTCAACTTCTCCCTGATGACGGAGCTGAGCATCAAGAGCGGCAACCCCGGGA  
GTCC'TCCCGCGGCTGGATGTGGGGCTGCGCCCTTCTCGGGGACTCCAGTACATCGTCACTGCTTCTCC'TCGGACAACTGG  
CCCGGCTCTGGTGTGTGGAGACTGGAGAGATCAAGAGAGATATGGCGGCCACCAAGAGGCTGTGTGCTGCTTGGCC'TTC  
AATGACAGTGTGCTGGGCTAG



Figure 10

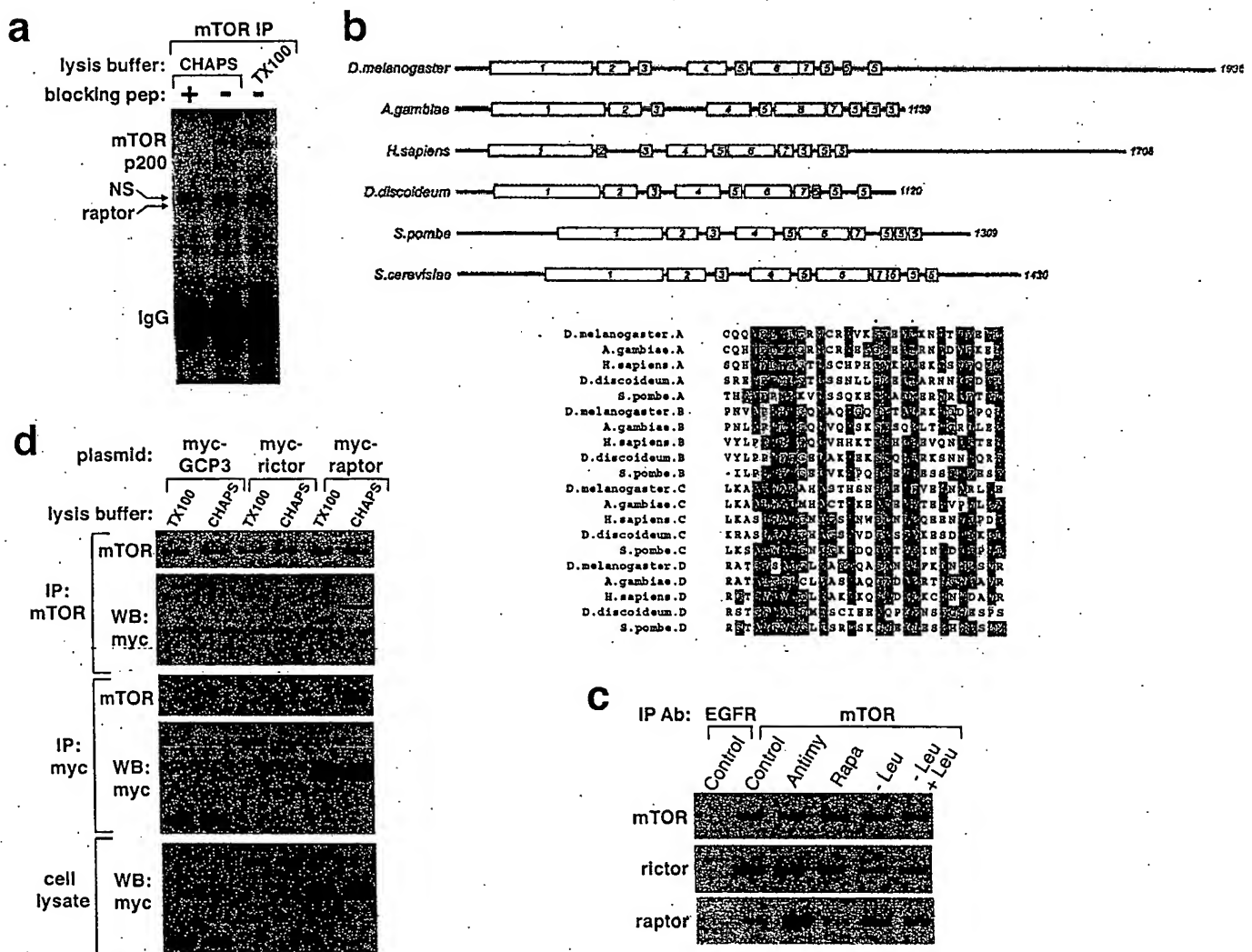
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GβL amino acid sequence (accession # AAH17119)

MNTSPGTVGSDPVILATAGYDHTVRFWQAHSGICTRTVQHQDSQVNALEVTTPDRSMIAAAGYQHIRMVYDLNSNNPNPIIS  
YDGVNKNIASVGFHEDGRWMTGGEDCTARIWDLRSRNLCQRIQVNAFINCVCLHPNQAELIVGDQSGAIHIWDLKTD  
HNEQLIPEPEVSITSAHIDPDASYMAAVNSTGNCYVWNL<sup>1</sup>TGGIGDEVTQLIPKTKIPAHTRYALQCRFSPDSTLLATCSA  
DQTCKIWRTSNFSLMTELSIKSGNPGESSRGWMMWGCAFSGDSQYIVTGEPRPGLPHPWPPALASRASPPRLQLPLCWGRL  
LGLHLRS.

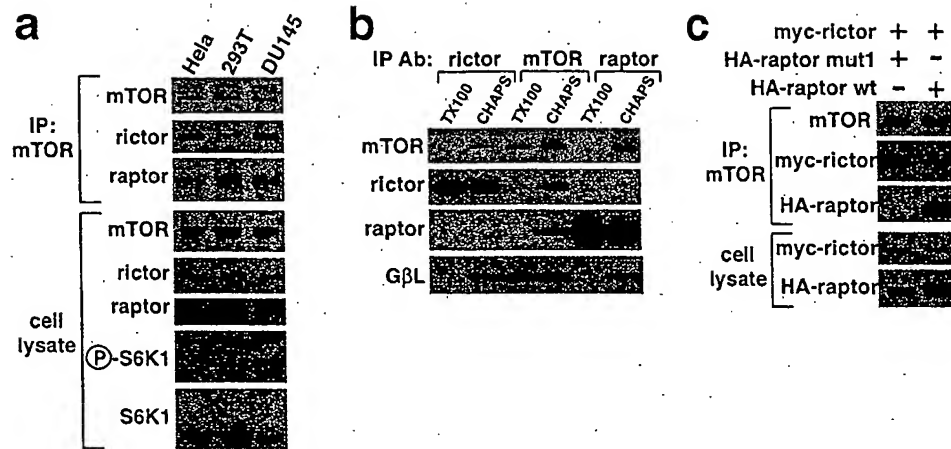
11

Figure 11



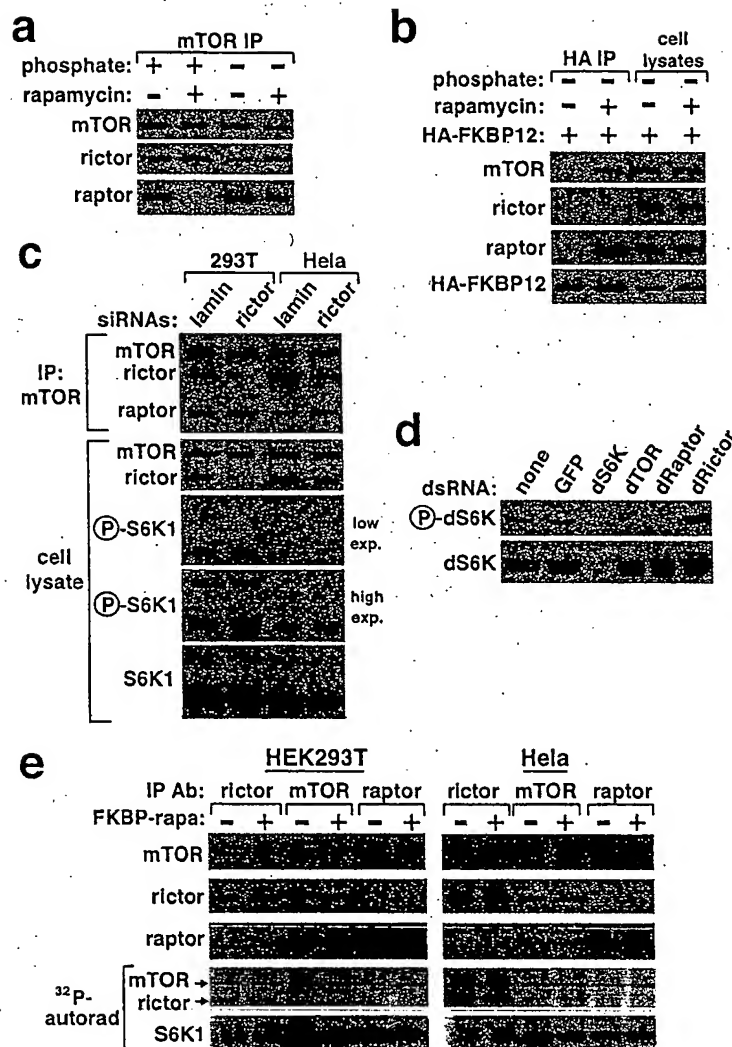
**Rictor is a novel mTOR-associated protein.** **a**, Silver stain of SDS-PAGE analysis of mTOR immunoprecipitates prepared from HeLa cells lysed in a CHAPS- or Triton X-100-containing buffer. (+) indicates inclusion of the blocking peptide for the mTOR antibody during the immunoprecipitation. The ~200 kDa band corresponds to rictor and a non-specific band (NS) obscures raptor. **b**, Rictor homologues share common domain architectures. Analyses of indicated rictor homologues identified seven domains with sequence conservation and similar relative locations within each protein and are shown schematically as boxes. Domain five is repeated four times within each of the homologues and the multiple sequence alignment shows the sequence pattern of this repeat. **c**, Specific interaction between endogenous mTOR and rictor. Immunoprecipitates prepared with the indicated antibodies were analyzed by immunoblotting for mTOR, rictor and raptor. Prior to use cells were treated with 5  $\mu$ M Antimycin A for 15 min (Antimy), 20 nM rapamycin for 15 min (Rapa), deprived of leucine for 90 min (-Leu), or deprived of leucine and stimulated with 52  $\mu$ g/ml leucine for 10 min (-Leu+Leu). **d**, Endogenous mTOR interacts with recombinant rictor and raptor. Cellular lysates and mTOR immunoprecipitates prepared from HEK293T cells expressing myc-rictor, myc-raptor, or myc-GCP3 were analyzed by immunoblotting for myc-tagged proteins. In parallel, anti-myc immunoprecipitates were analyzed by immunoblotting for mTOR.

**Figure 12**



**Rictor and raptor define two distinct mTOR-containing complexes.** **a**, Immunoblot analyses for indicated proteins of mTOR immunoprecipitates and cell lysates prepared from HeLa, HEK293T, and DU145 cells. Equal amounts of total protein were analyzed from each cell type. **b**, Immunoblot analyses for the presence of the indicated components of the mTOR signaling complex in immunoprecipitates prepared from HEK293T cell lysates with antibodies against rictor, mTOR, or raptor. **c**, Recombinant wild type raptor but not a mutant raptor suppresses the binding of rictor to mTOR. mTOR immunoprecipitates prepared from HEK293T cells expressing the indicated tagged proteins were analyzed by immunoblotting with anti-myc and anti-HA antibodies.

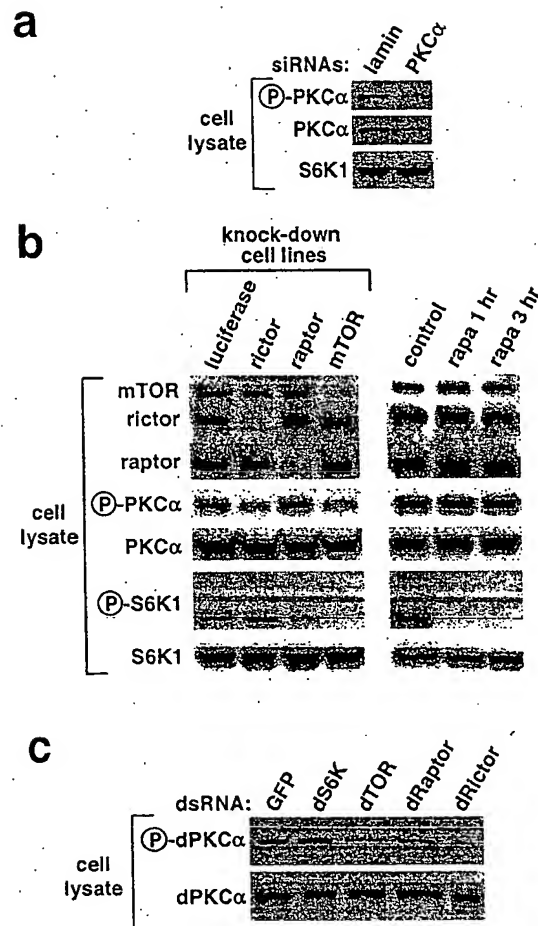
Figure 13



**Rictor does not participate in rapamycin-sensitive mTOR functions.**

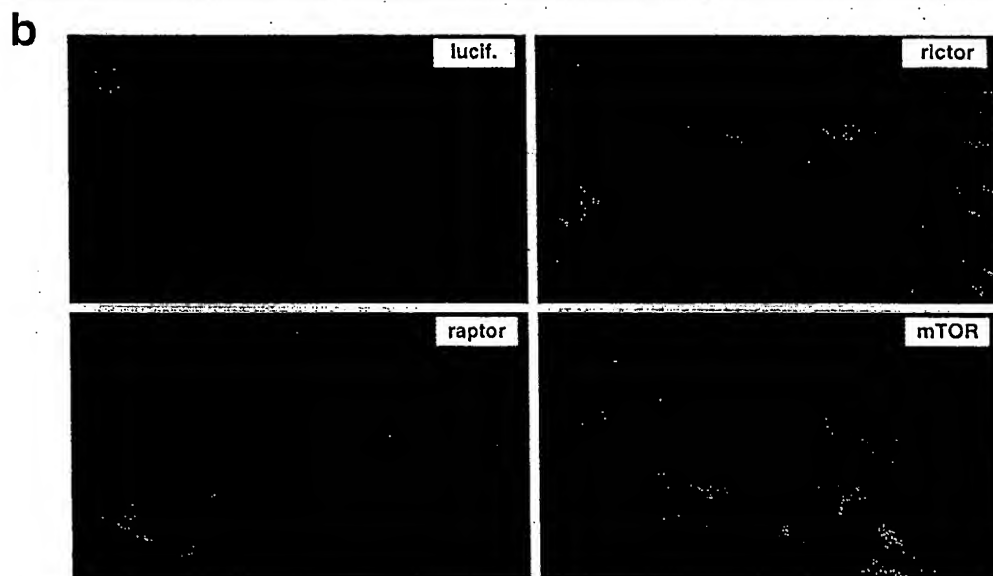
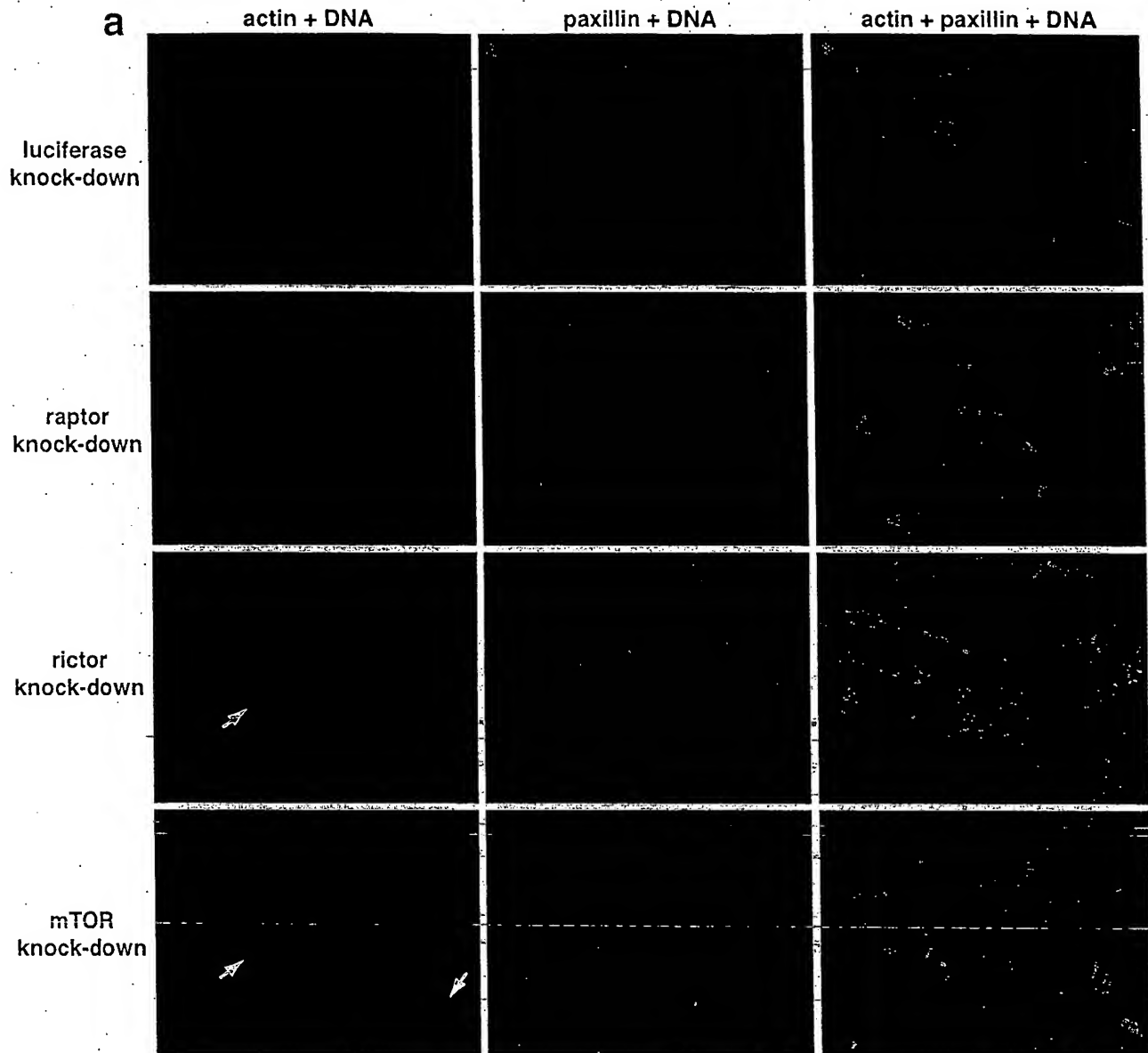
**a**, The sensitivity of the raptor-mTOR interaction to rapamycin depends on the presence of phosphate-containing molecules in the lysis buffer. mTOR immunoprecipitates prepared from cells treated with or without 20 nM rapamycin for 10 min and lysed in a phosphate-containing or phosphate-free buffer were analyzed by immunoblotting for the indicated proteins. **b**, Raptor and mTOR, but not rictor, co-purify with FKBP12-rapamycin. Anti-HA immunoprecipitates prepared from HEK293T cells expressing HA-FKBP12 and treated with or without 20 nM rapamycin for 15 min were analyzed by immunoblotting for the indicated proteins. **c**, Suppression of rictor expression slightly increases the amount of raptor in the mTOR complex and S6K1 activity. mTOR immunoprecipitates and cell lysates prepared from HEK293T or HeLa cells transfected with siRNAs targeting lamin or rictor were analyzed by immunoblotting for the indicated proteins. **d**, Suppression of Drosophila rictor expression increases the phosphorylation state of dS6K. The indicated dsRNAs were applied to Drosophila S2 cells and cell lysates were analyzed by immunoblotting with the mammalian phospho-specific S6K1 and Drosophila S6K antibodies. **e**, The rictor-containing mTOR complex does not phosphorylate S6K1. Immunoprecipitates prepared with the indicated antibodies were used in mTOR kinase assays using S6K1 as a substrate<sup>1</sup>. Where indicated immunoprecipitates were treated with 100 nM FKBP12-rapamycin for 40 min before the start of the assays. Immunoblotting was used to monitor the levels of rictor, mTOR, and raptor in the kinase reactions.

**Figure 14**

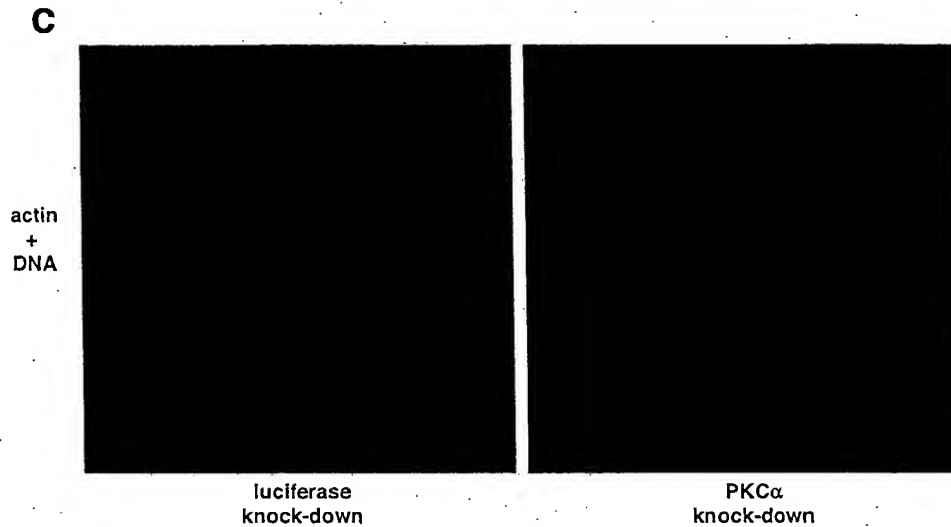


**Rictor and mTOR, but not raptor, regulate the PKCα phosphorylation state in human and Drosophila cells.** **a**, siRNA-mediated reduction in the expression of total PKCα in HeLa cells also reduces the immunoblot signal from a phosphospecific antibody recognizing phospho-S657 of PKCα but does not affect the levels of S6K1. **b**, Immunoblotting was used to analyze the phosphorylation states of PKCα and S6K1 in HeLa cells with reduced expression of rictor, raptor, or mTOR or treated with rapamycin. Lentiviruses were used to express siRNAs targeting rictor, raptor, mTOR or luciferase. **c**, dsRNAs corresponding to the genes for the indicated proteins were applied to S2 Drosophila cells. After 4 days lysates were prepared and analyzed by immunoblotting for dPKCα and phospho-dPKCα levels.

Figure 15ab

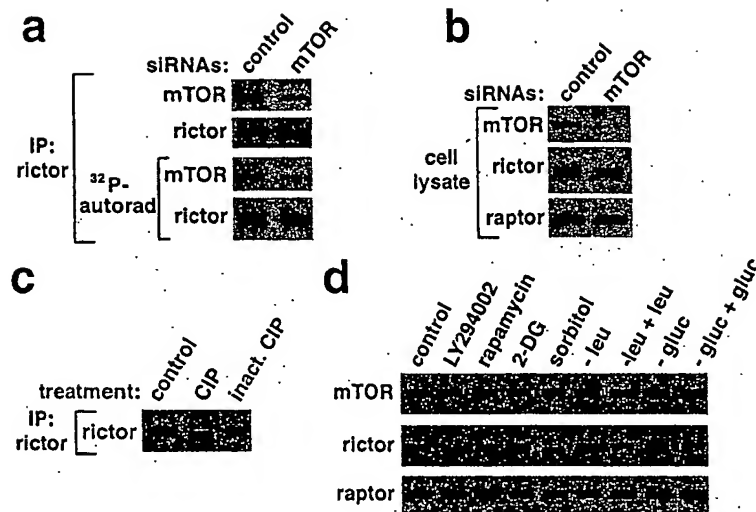


**Figure 15c**



Rictor, mTOR and PKC $\alpha$  regulate the organization of the actin cytoskeleton. a, Staining for actin (red), paxillin (green) and DNA (blue) reveals the organization of the actin cytoskeleton in HeLa cells transduced with the siRNA-expressing lentiviruses described in Figure 4a. Arrows point to bundles of actin fibers. Images captured with a 60x objective are shown. b, Higher magnification of portions of the merged images from Figure 5a. c, Like cells with reduced rictor expression, cells with reduced expression of PKC $\alpha$  have an altered actin cytoskeleton.

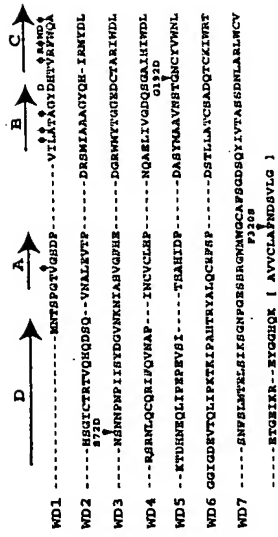
**Figure 16**



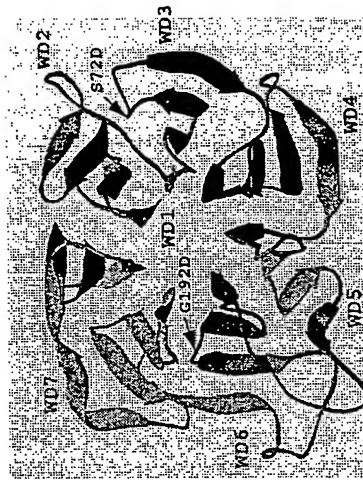
mTOR regulates the rictor phosphorylation state. **a**, HeLa cells with reduced expression of mTOR or of a control protein were metabolically labeled with  $^{32}\text{P}$  and the level of phosphorylated rictor determined by immunoprecipitation followed by autoradiography and immunoblotting for the indicated proteins. **b**, The mobility of rictor in SDS-PAGE is affected by mTOR. HeLa cells with siRNA-mediated reductions in mTOR or controls were analyzed by immunoblotting for mTOR, rictor, and raptor. **c**, The phosphorylation state of rictor affects its mobility in SDS-PAGE. Rictor immunoprecipitates were incubated with or without calf intestinal phosphatase (CIP) or heat inactivated CIP and analyzed by SDS-PAGE and immunoblotting for rictor. **d**, Osmotic stress increases the mobility of rictor in SDS-PAGE. Lysates of HeLa cells exposed for 1 hr to 20 nM rapamycin, 20 nM LY294002, 100 mM 2 deoxyglucose (2-DG), medium without leucine or glucose, or medium without leucine or glucose followed by the readdition of the missing component for 10 minutes were analyzed by immunoblotting for rictor.



## Figure 17



## Figure 18



## Figure 19

